ABSTRACT

Charles University in Prague

Faculty of Pharmacy in Hradci Králové

Deparment of Inorganic and Organic Chemistry

Candidate: Ondřej Tesař

Supervisor: doc. PharmDr. Kateřina Vávrová, Ph.D.

Title of diploma thesis: Synthesis of phytoceramide analogues and evaluation of their effect on the skin barrier properties.

Phytoceramides (FCER) belong to the class of sphingolipids. They are composed of a basic alcohol phytosphingosine (P) and the acyl chain. Together with the other lipids they create the extracellular membrane in human stratum corneum (SC), the uppermost layer of the skin, which protects us against the loss of water and penetration of foreign compounds into our body. The influence of FCER structure on the function of this membrane is unknown yet.

Aim of the work: The aim of this work was to examine what role the acyl chain length of FCER plays in this membrane impermeability.

Methods: My task was to synthetize FCER with acyl chain length of 2, 4, 6 and 24 carbons and preparation of SC model membranes containing FCER with acyl chain length of 2, 4, 6, 8 or 24 carbons, cholesterol, lignoceric acid and cholesterol sulfate.
The permeabilities of the model membranes were evaluated in Franz diffusion cells. Electric impedance and permeability for two model drugs: theophylline (TH) and indomethacin (IND), which were determined by high performance liquid chromatography (HPLC).

Main findings: We discovered that the membranes with short acyl chain FCER are several times more permeable than the control membranes with the physiological FCER with acyl chain length of 24 carbons. The most permeable membrane was the one containing 4 carbons acyl analogue (approximately 2,7 times more for ions, 10,5 times for TH, 2,8 times for IND rather than control). Thus, sufficient acyl chain length in FCER is necessary to maintain their

skin barrier properties similar as for ceramides (CER) derived from sphingosine (S) and dihydrosphingosine (DS).

The influence of the polar head structure of CER on their barrier properties was studied in the second part of this work. Model membranes composed of CER derived from P, DS, S and synthetic analogue tetradecyltetracosanoyl-*L*-serinate (14S24) with equal chain length were prepared. The membranes were evaluated the same way as membranes made of FCER. We discovered that the permeability of the membranes were comparable, only the permeability for TH of membrane 14S24 was significantly higher.

Conclusinon: This work is the first step for clarification of the influence of FCER structure on the skin barrier properties and will be foundation for further research.

Keywords: phytoceramide, stratum corneum, model membrane, NP